

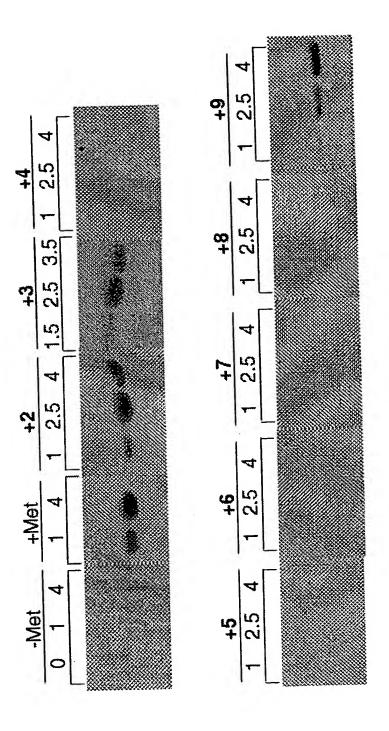
DNA

ACID ANALOGUES
Application No.: Unassigned Filing Date: July 1, 2003
Docket No.: CIT1460-2

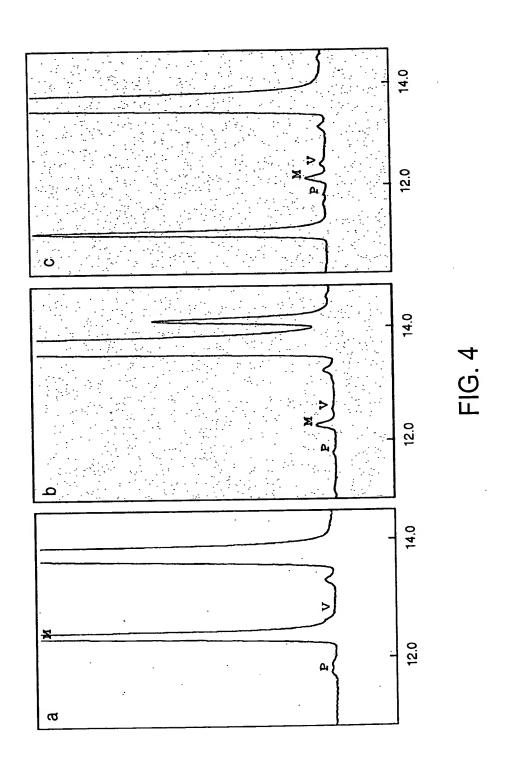
2/28

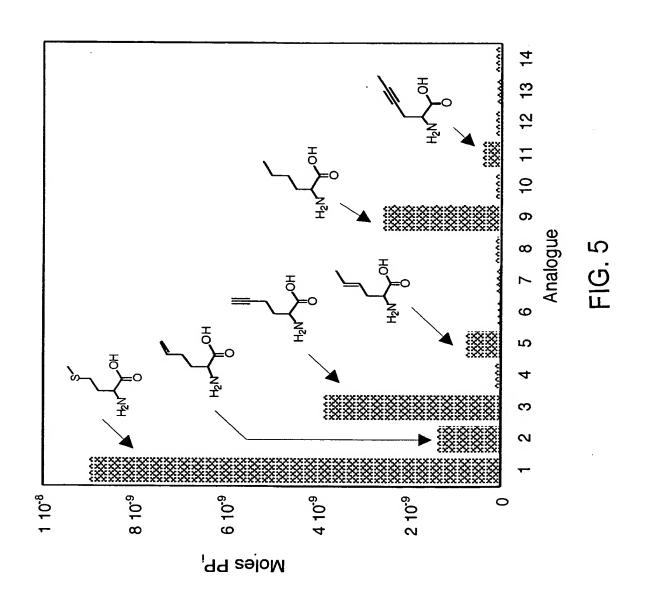
- 1. Methionine
- 2. Homoallylglycine
- 3. Homopropargylglycine
- 4. Cis-crotylglycine
- 5. Trans-crotylglycine
- 6. 6,6,6-trifluoro-2-amino hexanoic acid
- 7. 2-amino heptanoic acid
- 8. Norvaline
- 9. Norleucine
- 10. o-allylserine
- 11. 2-butynylglycine
- 12. Allylglycine
- 13. Propargylglycine

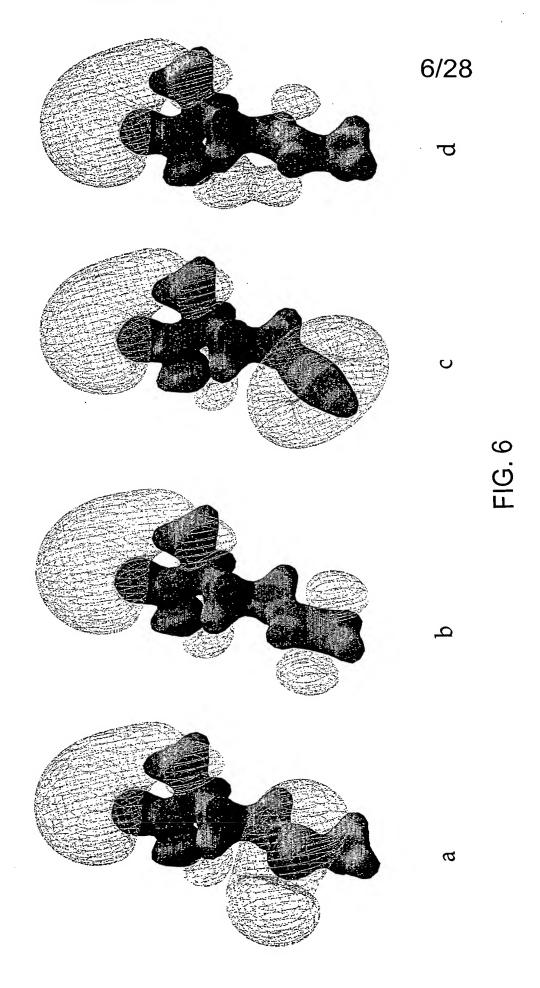
FIG. 2



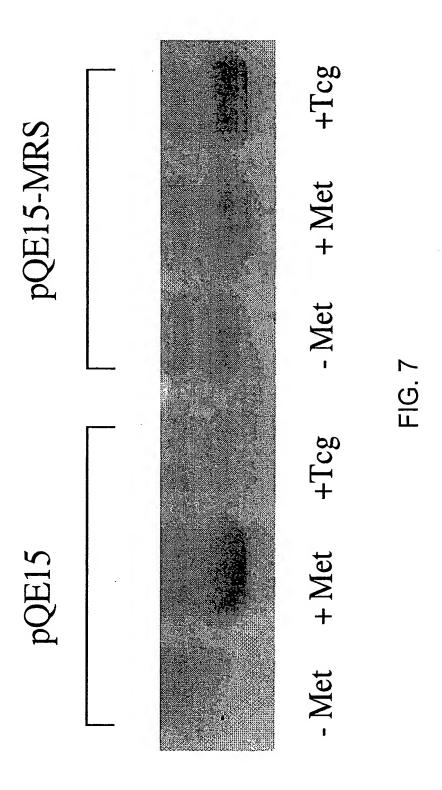
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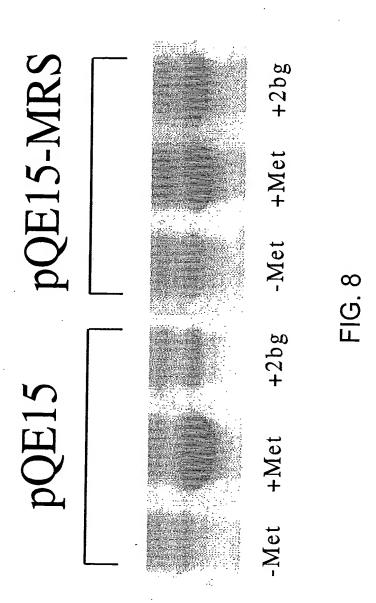






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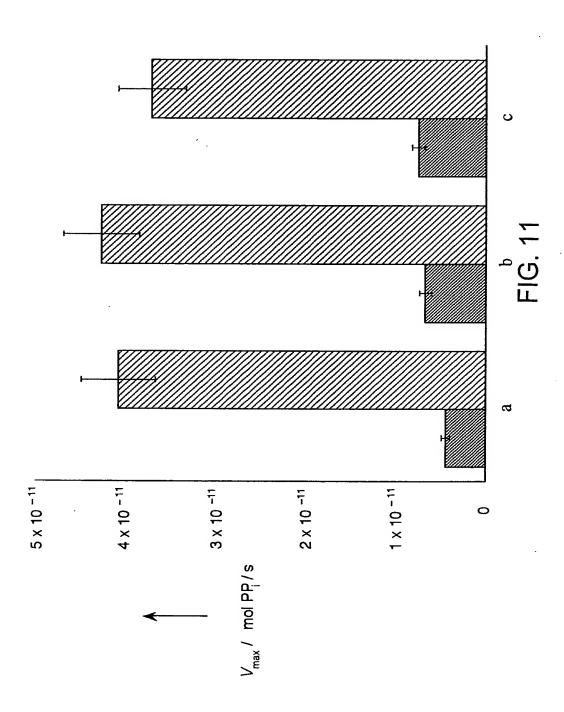




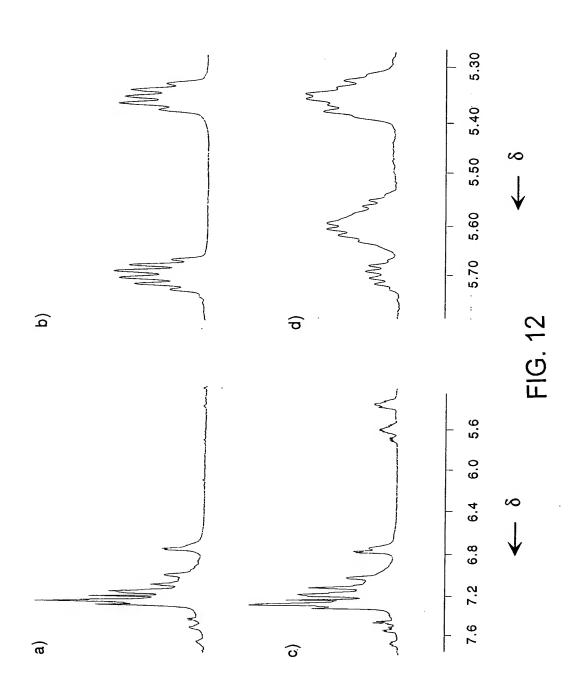
- Met

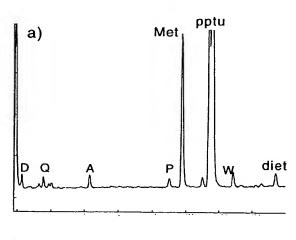
pQE15 pQE15-MRS

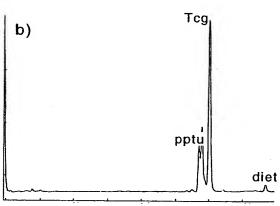
| Incorporated by conventional host?     | ¥                       | ¥                 | X                       | X          | Y          | Z                  | Z                      | Z                      | Z                      | Z                       |
|--|-------------------------|-------------------|-------------------------|------------|------------|--------------------|------------------------|------------------------|------------------------|-------------------------|
| Relative<br>Value                      | 1                       | 1/390             | 1 / 500                 | 1 / 1050   | 1 / 1850   | 1 / 4700           | 1/13825                | 1/46100                | 1/171000               | 1/456000                |
| $\rm k_{cat}/K_m$ $(s^{-1}\mu M^{-1})$ | 5.47 x 10 <sup>-1</sup> | $1.4 \times 10^3$ | 1.08 x 10 <sup>-3</sup> | 5.22 x 10⁴ | 2.96 x 10⁴ | $1.16 \times 10^4$ | 3.9 x 10 <sup>-5</sup> | 1.2 x 10 <sup>-5</sup> | 3.2 x 10 <sup>-6</sup> | .1.2 x 10 <sup>-6</sup> |
| (u                                     | 8                       | <del></del>       | ,z                      | _          | /          |                    |                        | ر -                    |                        | الم                     |
| Analogue<br>(Side chain shown)         | Met                     | Aha               | Hpg                     | Norl       | Hag        | Tcg                | 2bg                    | Norv                   | Ccg                    | Ag                      |



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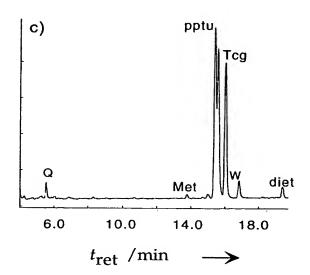
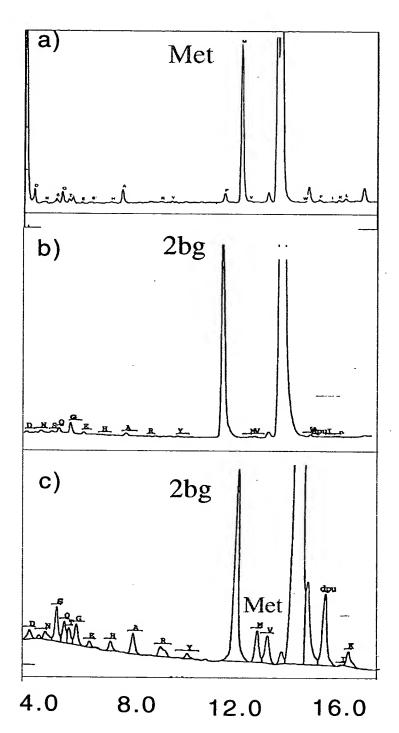


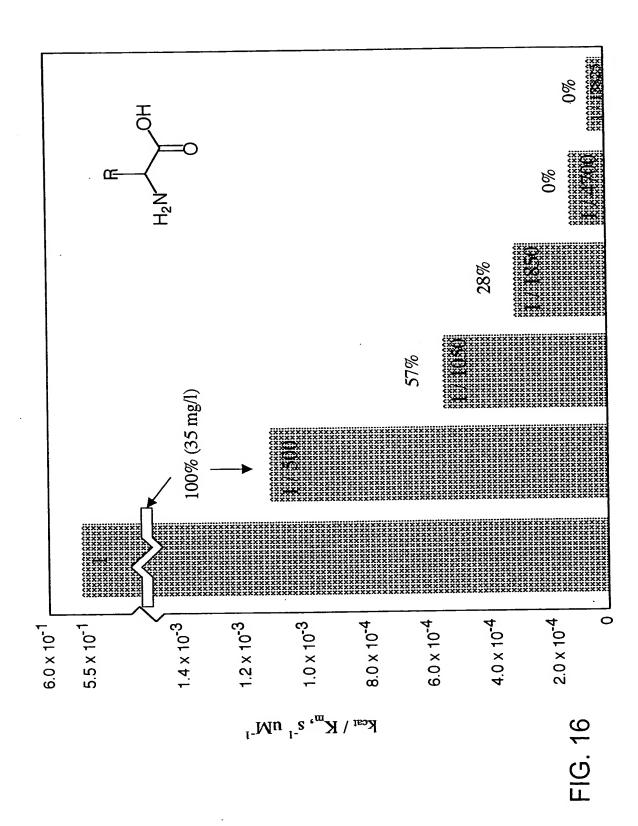
FIG. 13



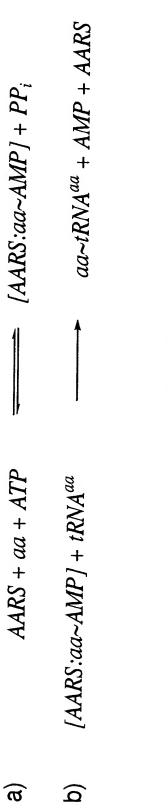
Retention time, minutes

FIG. 14

| Analogue | K <sub>m</sub> (µM) | $k_{cat}(s^{-1})$ | $k_{cat}(s^{-1}) = k_{cat}/K_m(s^{-1}\mu M^{-1})$ | Protein Yield, mg/L |     |
|----------|---------------------|-------------------|---|---------------------|-----|
| 1        | 24.3 ± 2            | 13.3 ± 0.2        | 5.47x10 <sup>-1</sup>                             | 35                  |     |
| က        | $2415 \pm 170$      | $2.60 \pm 0.3$    | $1.08 \times 10^{-3}$                             | 35                  |     |
| 6        | $4120 \pm 900$      | $2.15 \pm 0.6$    | $5.22 \times 10^{-4}$                             | 20                  | 15/ |
| 7        | $4555 \pm 200$      | $1.35 \pm 0.1$    | 2.96x10 <sup>-4</sup>                             | 10                  | 28  |
| w        | $15,675 \pm 250$    | $1.82 \pm 0.6$    | $1.16x10^{-4}$                                    | 0                   |     |
|          |                     |                   |   |                     |     |







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| CTCGAGAAAT | AT CATAAAAAT         | I TTATTTGCTT | TGTGAGCGGA | TAACAATTAT | AATAGATTCA | 09   |
|------------|----------------------|--------------|------------|------------|------------|------|
| ATTGTGAGCG | CG GATAACAAT         | I TCACACAGAA | TTCATTAAAG | AGGAGAAATT | AACTATGAGA | 120  |
| GGATCGCATC | IC ACCATCACCA        | A TCACGGATCC | GGCATCATGG | TTCGACCATT | GAACTCGATC | 180  |
| GICCCCGIGI | CCCAAAATA            | T GGGGATTGGC | AAGAACGGAG | ACCTACCCTG | GCCTCCGCTC | 240  |
| AGGAACGAGT | ST TCAAGTACTT        | I CCAAAGAATG | ACCACAACCT | CTTCAGTGGA | AGGTAAACAG | 300  |
| AATCTGGTGA | SA TTATGGGTAG        | 3 GAAAACCTGG | TTCTCCATTC | CTGAGAAGAA | TCGACCTTTA | 360  |
| AAGGACAGAA | AA TTAATATAGT        | I TCTCAGTAGA | GAACTCAAAG | AACCACCACG | AGGAGCTCAT | 420  |
| TTTCTTGCCA | CA AAAGTTTGGA        | A TGATGCCTTA | AGACTTATTG | AACAACCGGA | ATTGGCAAGT | 480  |
| AAAGTAGACA | TGGTTTGGA            | T AGTCGGAGGC | AGTICIGITI | ACCAGGAAGC | CATGAATCAA | 540  |
| CCAGGCCACC | TTAGACTCT            | T TGTGACAAGG | ATCATGCAGG | AATTTGAAAG | TGACACGITI | 009  |
| TTCCCAGAAA | AA TTGATTTGGG        | S GAAATATAAA | CTTCTCCCAG | AATACCCAGG | CGTCCTCT   | 099  |
| GAGGTCCAGG | SG AGGAAAAAGG        | 3 CATCAAGTAT | AAGTTTGAAG | TCTACGAGAA | GAAAGGTTGG | 720  |
| AAGATCTTAA | AA GCTTAATTAG        | 3 CTGAGCTTGG | ACTCCTGTTG | ATAGATCCAG | TAATGACCTC | 780  |
| AGAACTCCAT | AT CTGGATTTGT        | I TCAGAACGCT | CGGTTGCCGC | CGGGCGTTTT | TTATTGGTGA | 840  |
| GAATCCAAGC | SC TAGCTCTAGA        | A GACGICCGGC | CGGAGCTCCA | CCGCGGTGGC | GGCCGCTCTA | 006  |
| GAGTCACTTA | LA CTTAACATT         | r TCCCATTTGG | TACTATCTAA | CCCCTTTTCA | CTATTAAGAA | 960  |
| GTAATGCCTA | IA CTATGACTCA        | A AGTCGCGAAG | AAAATTCTGG | TGACGTGCGC | ACTGCCGTAC | 1020 |
| GCTAACGGCT | CT CAATCCACCT        | r cggccatatg | CTGGAGCACA | TCCAGGCTGA | TGTCTGGGTC | 1080 |
| CGITACCAGC | SC GAATGCGCGG        | S CCACGAGGIC | AACTTCATCT | GCGCCGACGA | TGCCCACGGT | 1140 |
| ACACCGATCA | CA TGCTGAAAGC        | C TCAGCAGCIT | GGTATCACCC | CGGAGCAGAT | GATTGGCGAA | 1200 |
| ATGAGTCAGG | SG AGCATCAGAC        | C TGATTTCGCA | GGCTTTAACA | TCAGCTATGA | CAACTATCAC | 1260 |
| TCGACGCACA | CA GCGAAGAGAA        | A CCGCCAGTIG | TCAGAACTTA | TCTACTCTCG | CCTGAAAGAA | 1320 |
| AACGGTTTTA | <b>FA TTAAAAACCG</b> | S CACCATCTCT | CAGCTGTACG | ATCCGGAAAA | AGGCATGTTC | 1380 |
| CTGCCGGACC | C GTTTTGTGAA         | A AGGCACCIGC | CCGAAATGTA | AATCCCCGGA | TCAATACGGC | 1440 |
| GATAACTGCG | SG AAGTCTGCGG        | 3 CGCGACCTAC | AGCCCGACTG | AACTGATCGA | GCCGAAATCG | 1500 |
| GIGGTITCIG | re ecectacecc        | C GGTAATGCGT | GATTCTGAAC | ACTICTICTT | TGATCTGCCC | 1560 |

# FIG. 19-1

| GGCATGGACC |
|------------|
| TGAATCTGGC |
| TCCGAACGCG |
| TTCTTTCAAG |
| GAAAGACTCC |
| CCTGTTCTGG |
| TCATGGCTAT |
| AGCCAGCACC |
| ACTCTCTTCG |
| TGCCGATATC |
| GCGTTTTGAC |
| TGATGCCGCT |
| CGAAATCATG |
| GGTGGCGAAA |
| CCTGTTCCGC |
| AGAAGCATTC |
| CAAAGTGAAT |
| GGTGGAAGCC |
| AGATGATCCG |
| GGCGCTGATT |
| GGATCTCGGC |
| GCAGGCACTG |
| CTTCGGTAT  |
| GCTAAGCCC  |
| GCTGCATCGA |
| CTCTCTAACC |

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| CTGGATAAAA<br>TAAATTCAGG | TTACAGGGAT<br>GCAGTTGAGC | GCAGAATGAG<br>AACAGGGAAA | ACACTTTATC<br>CGAGTTGCAT | TATCAGGACG<br>ATCAGTTGGG | AAAAATCACA<br>GAAAAGTTGG | 3180<br>3240 |
|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------|
| CACCAAAGGC               | AAAGCCAGAT               | AAAAAGTTTT               | TCAGATGCTG               | CGGCAGCGGC               | AAAAGCGGAG               | 3300         |
| CCCGACCTCG               | AGGGGGGGCC               | CGGTACCCGG               | CCGGACGICI               | CTAGAGCTAG               | CTTGGCGAGA               | 3360         |
| TTTTCAGGAG               | CTAAGGAAGC               | TAAAATGGAG               | AAAAAATCA                | CTGGATATAC               | CACCGTTGAT               | 3420         |
| ATATCCCAAT               | GGCATCGTAA               | AGAACATTTT               | GAGGCATTTC               | AGTCAGTTGC               | TCAATGTACC               | 3480         |
| TATAACCAGA               | CCGTTCAGCT               | GGATATTACG               | GCCTTTTTAA               | AGACCGTAAA               | GAAAAATAAG               | 3540         |
| CACAAGTTTT               | ATCCGGCCTT               | TATTCACATT               | CIIGCCCCCC               | TGATGAATGC               | TCATCCGGAA               | 3600         |
| TTTCGTATGG               | CAATGAAAGA               | CGGTGAGCTG               | GTGATATGGG               | ATAGTGTTCA               | CCCTTGTTAC               | 3660         |
| ACCGTTTTCC               | ATGAGCAAAC               | TGAAACGTTT               | TCATCGCTCT               | GGAGTGAATA               | CCACGACGAT               | 3720         |
| TTCCGGCAGT               | TTCTACACAT               | ATATTCGCAA               | GATGTGGCGT               | GTTACGGTGA               | AAACCTGGCC               | 3780         |
| TATTTCCCTA               | AAGGGTTTAT               | TGAGAATATG               | TTTTTCGTCT               | CAGCCAATCC               | CTGGGTGAGT               | 3840         |
| TICACCAGIT               | TTGATTTAAA               | CGTGGCCAAT               | ATGGACAACT               | TCTTCGCCCC               | CGTTTTCACC               | 3900         |
| ATGGGCAAAT               | ATTATACGCA               | AGGCGACAAG               | GTGCTGATGC               | CGCTGGCGAT               | TCAGGTTCAT               | 3960         |
| CATGCCGTCT               | GTGATGGCTT               | CCATGTCGGC               | AGAATGCTTA               | ATGAATTACA               | ACAGTACTGC               | 4020         |
| GATGAGTGGC               | AGGGCGGGGC               | GTAATTTTT                | TAAGGCAGTT               | ATTGGTGCCC               | TTAAACGCCT               | 4080         |
| GGGGTAATGA               | CTCTCTAGCT               | TGAGGCATCA               | AATAAAACGA               | AAGGCTCAGT               | CGAAAGACTG               | 4140         |
| GGCCTTTCGT               | TTTATCTGTT               | GTTTGTCGGT               | GAACGCTCTC               | CTGAGTAGGA               | CAAATCCGCC               | 4200         |
| GCTCTAGAGC               | TGCCTCGCGC               | GTTTCGGTGA               | TGACGGTGAA               | AACCTCTGAC               | ACATGCAGCT               | 4260         |
| CCCGGAGACG               | GTCACAGCTT               | GTCTGTAAGC               | GGATGCCGGG               | AGCAGACAAG               | CCCGTCAGGG               | 4320         |
| CGCGTCAGCG               | GGTGTTGGCG               | GGTGTCGGGG               | CGCAGCCATG               | ACCCAGICAC               | GTAGCGATAG               | 4380         |
| CGGAGTGTAT               | ACTGGCTTAA               | CTATGCGGCA               | TCAGAGCAGA               | TTGTACTGAG               | AGTGCACCAT               | 4440         |
| ATGCGGTGTG               | AAATACCGCA               | CAGATGCGTA               | AGGAGAAAAT               | ACCGCATCAG               | GCGCICIICC               | 4500         |
| GCTTCCTCGC               | TCACTGACTC               | GCTGCGCTCG               | GICIGICGGC               | TGCGGCGAGC               | GGTATCAGCT               | 4560         |
| CACTCAAAGG               | CGGTAATACG               | GTTATCCACA               | GAATCAGGGG               | ATAACGCAGG               | AAAGAACATG               | 4620         |
| TGAGCAAAAG               | GCCAGCAAAA               | GGCCAGGAAC               | CGTAAAAAGG               | CCGCGTTGCT               | GGCGTTTTTC               | 4680         |

# FIG. 19-3

| 4          | 4800       | 4860       | 4920       | 4980       | 5040       | 5100       | 5160       | 5220       | 5280       | 5340       | 5400       | 5460       | 5520       | 5580       | 5640       | 5700       | 5760       | 5820       | 5880       | 5940       | 0009       | 0909       | 6120       | 6180       | 6240       |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| GAGGTGGCGA | CGTGCGCTCT | GGGAAGCGTG | TCGCTCCAAG | CGGTAACTAT | CACTGGTAAC | GIGGCCIAAC | AGTTACCTTC | CGGTGGTTTT | TCCTTTGATC | TTTGGTCATG | TTTTAAATCA | CAGTGAGGCA | CGTCGTGTAG | ACCGCGAGAC | GGCCGAGCGC | CCGGGAAGCT | TACAGGCATC | ACGATCAAGG | TCCTCCGATC | ACTGCATAAT | CTCAACCAAG | AATACGGGAT | TTCTTCGGGG | CACTCGTGCA | AAAAACAGGA |
| GCTCAAGTCA | GAAGCTCCCT | TICICCCIIC | TGTAGGTCGT | GCGCCTTATC | TGGCAGCAGC | TCTTGAAGTG | TGCTGAAGCC | CCGCTGGTAG | CTCAAGAAGA | GTTAAGGGAT | AAAAATGAAG | AATGCTTAAT | CCIGACICCC | CTGCAATGAT | CAGCCGGAAG | TTAATTGTTG | TIGCCATIGC | CCGGTTCCCA | GCICCIICGG | TTATGGCAGC | CTGGTGAGTA | CCCCGCCGIC | TTGGAAAACG | CGATGTAACC | CIGGGIGAGC |
| AAAAATCGAC | TTTCCCCCTG | CIGICCECCI | CTCAGTTCGG | CCCGACCGCT | TTATCGCCAC | GCTACAGAGT | ATCTGCGCTC | AAACAAACCA | AAAAAAGGAT | GAAAACTCAC | CTTTTAAATT | GACAGTTACC | TCCATAGCTG | GGCCCCAGTG | ATAAACCAGC | ATCCAGTCTA | CGCAACGTTG | TCATTCAGCT | AAAGCGGTTA | TCACTCATGG | TTTTCTGTGA | AGTIGCICIT | GTGCTCATCA | AGATCCAGTT | ACCAGCGITI |
| CGAGCATCAC | ATACCAGGCG | TACCGGATAC | CTGTAGGTAT | CCCCGTTCAG | AAGACACGAC | TGTAGGCGGT | AGTATTTGGT | TTGATCCGGC | TACGCGCAGA | TCAGTGGAAC | CACCTAGATC | AACTTGGTCT | ATTTCGTTCA | CTTACCATCT | TTTATCAGCA | ATCCGCCTCC | TAATAGTTTG | TGGTATGGCT | GTTGTGCAAA | CGCAGTGTTA | CGTAAGATGC | GCGCCGACCG | AACTTTAAAA | ACCGCTGTTG | TTTTACTTTC |
| GCCCCCTGA  | GACTATAAAG | CCCTGCCGCT | AATGCTCACG | TGCACGAACC | CCAACCCGGT | GAGCGAGGTA | CTAGAAGGAC | TTGGTAGCTC | AGCAGCAGAT | GGTCTGACGC | AAAGGATCTT | TATATGAGTA | CGATCTGTCT | TACGGGAGGG | CGGCTCCAGA | CTGCAACTTT | GTTCGCCAGT | GCTCGTCGTT | GATCCCCCAT | GTAAGTTGGC | TCATGCCATC | AATAGTGTAT | CACATAGCAG | CAAGGATCTT | CTTCAGCATC |
| CATAGGCTCC | AACCCGACAG | CCTGTTCCGA | GCGCTTTCTC | CIGGGCIGIG | CGTCTTGAGT | AGGATTAGCA | TACGGCTACA | GGAAAAAGAG | TTTGTTTGCA | TTTTCTACGG | AGATTATCAA | ATCTAAAGTA | CCTATCTCAG | ATAACTACGA | CCACGCTCAC | AGAAGTGGTC | AGAGTAAGTA | GIGGIGICAC | CGAGTTACAT | GTTGTCAGAA | TCTCTTACTG | TCATTCTGAG | AATACCGCGC | CGAAAACTCT | CCCAACTGAT |
|            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |

| 6501 |               |            |            | Ü          | TICGICTICA C  | ACGAGGCCCT   |
|------|---------------|------------|------------|------------|---|--------------|
| 6480 | TAGGCGTATC    | CCTATAAAAA | ATGACATTAA | CATTATTATC | TCTAAGAAAC CATTATTATC ATGACATTAA CCTATAAAAA TAGGCGTATC 6480 | CCACCTGACG   |
| 6420 | CCGAAAAGTG    | GCACATTTCC | GGGGTTCCGC | TAAACAAATA | TITAGAAAAA TAAACAAATA GGGGTTCCGC GCACATTTCC CCGAAAAGTG 6420 | TTTGAATGTA   |
| 6360 | CGGATACATA    | GTCTCATGAG | CAGGGTTATT | AAGCATTTAT | AATATTATTG AAGCATTTAT CAGGGTTATT GTCTCATGAG CGGATACATA 6360 | TICCITITIC   |
| 9300 | ACT'CAT'ACT'C | AATGTTGAAT | GCGACACGGA | GGGAATAAGG | CCGCAAAAAA GGGAATAAGG GCGACACGGA AATGTTGAAT ACTCATACTC 6300 | AGGCAAAA'I'G |

| 1560 | GCCGAAAICG<br>TGATCTGCCC | AACIGAICGA | AGCCCGACTG<br>GATTCTGAAC | GGTAATGCGT | AAGTUTGUGG | GTGGTTTCTG |
|------|--------------------------|------------|--------------------------|------------|------------|------------|
| 4    | TCAATACGGC               | AATCCCCGGA | CCGAAATGTA               | AGGCACCTGC | GTTTTGTGAA | CTGCCGGACC |
| 1380 | AGGCATGTTC               | ATCCGGAAAA | CAGCTGTACG               | CACCATCTCT | TTAAAAACCG | AACGGTTTTA |
| 1320 | CCTGAAAGAA               | TCTACTCTCG | TCAGAACTTA               | CCGCCAGTIG | GCGAAGAGAA | TCGACGCACA |
| 1260 | CAACTATCAC               | TCAGCTATGA | GGCTTTAACA               | TGATTTCGCA | AGCATCAGAC | ATGAGTCAGG |
| 1200 | GATTGGCGAA               | CGGAGCAGAT | GGTATCACCC               | TCAGCAGCTT | TGCTGAAAGC | ACACCGATCA |
| 1140 | TGCCCACGGT               | GCGCCGACGA | AACTTCATCT               | CCACGAGGTC | GAATGCGCGG | CGTTACCAGC |
| 1080 | TGTCTGGGTC               | TCCAGGCTGA | CTGGAGCACA               | CGGCCATATG | CAATCCACCT | GCTAACGGCT |
| 1020 | ACTGCCGTAC               | TGACGTGCGC | AAAATTCTGG               | AGTCGCGAAG | CTATGACTCA | GTAATGCCTA |
| 960  | CTATTAAGAA               | CCCCTTTTCA | TACTATCTAA               | TCCCATTTGG | CITAACAITI | GAGTCACTTA |
| 006  | GGCCGCTCTA               | CCGCGGTGGC | CGGAGCTCCA               | GACGTCCGGC | TAGCTCTAGA | GAATCCAAGC |
| 840  | TTATTGGTGA               | CGGGCGTTTT | CGGTTGCCGC               | TCAGAACGCT | CTGGATTTGT | AGAACTCCAT |
| 780  | TAATGACCTC               | ATAGATCCAG | ACTCCTGTTG               | CTGAGCTTGG | GCTTAATTAG | AAGATCTTAA |
| 720  | GAAAGGTTGG               | TCTACGAGAA | AAGTTTGAAG               | CATCAAGTAT | AGGAAAAAGG | GAGGTCCAGG |
| 099  | CGICCICICI               | AATACCCAGG | CTTCTCCCAG               | GAAATATAAA | TTGATTTGGG | TTCCCAGAAA |
| 009  | TGACACGTTT               | AATTTGAAAG | ATCATGCAGG               | TGTGACAAGG | TTAGACTCTT | CCAGGCCACC |
| 540  | CATGAATCAA               | ACCAGGAAGC | AGTICIGITI               | AGTCGGAGGC | TGGTTTGGAT | AAAGTAGACA |
| 480  | ATTGGCAAGT               | AACAACCGGA | AGACTTATTG               | TGATGCCTTA | AAAGTTTGGA | TTTCTTGCCA |
| 420  | AGGAGCTCAT               | AACCACCACG | GAACTCAAAG               | TCTCAGTAGA | TTAATATAGT | AAGGACAGAA |
| 360  | TCGACCTTTA               | CTGAGAAGAA | TICICCATIC               | GAAAACCTGG | TTATGGGTAG | AATCTGGTGA |
| 300  | AGGTAAACAG               | CTTCAGTGGA | ACCACAACCT               | CCAAAGAATG | TCAAGTACTT | AGGAACGAGT |
| 240  | GCCICCGCIC               | ACCTACCCTG | AAGAACGGAG               | GGGGATTGGC | CCCAAAATAT | GICGCCGIGI |
| 180  | GAACTCGATC               | TICGACCATI | GGCATCATGG               | TCACGGATCC | ACCATCACCA | GGATCGCATC |
| 120  | AACTATGAGA               | AGGAGAAATT | TTCATTAAAG               | TCACACAGAA | GATAACAATT | ATTGTGAGCG |
| 09   | AATAGATTCA               | TAACAATTAT | TGTGAGCGGA               | TTATTTGCTT | CATAAAAAAT | CTCGAGAAAT |

| AAGTAAAAGC CGCTGCCGCG 2640 CCATCACCTT TGACGACTTC 2700 AGTTTGTTGA AGGTTCTGAC 2760 GCAATGTCTT CTCCGGTATT 2820 ACACCATTAT GGTGGCTAAC 2880 |
|--|
|  |
| CTCAATACGG CCGTTCAAGG CTCTAAATGAG ATTCAGGAAA CGAAAACGCAG CGTGAAAAACC   |
| AGAAGCATTC CAAAGCATTC CAAAGTGAAT GGTGGAAGCC AGATGATCCG GGCGCTGATT GGATCTCGGC   |
| CCGAGCGTGC TGCTGGGCCACT TTGAAGCACT GCCCGCTGGC ACCTGCGCGT ACCTGACGCT ACCCGGATCC   |
| CCGAAACTGA<br>CAGCAACCGC<br>ATGAGGCAGG<br>CCGGTAACTG<br>GCTAAAGTTG<br>AAACTGCTGC<br>CGTTCTGCTT   |

| CTGGATAAAA T  | TACAGGGAT  | GCAGAATGAG | ACACTTTATC | TATCAGGACG | AAAAATCACA | 3180 |
|---|------------|------------|------------|------------|------------|------|
|   | GCAGTTGAGC | AACAGGGAAA | CGAGTTGCAT | ATCAGTIGGG | GAAAAGTTGG | 3240 |
| Ø   | AAGCCAGAT  | AAAAAGTTTT | TCAGATGCTG | CGGCAGCGGC | AAAAGCGGAG | 3300 |
| K   | 225555555  | CGGTACCCGG | CCGGACGTCT | CTAGAGCTAG | CTTGGCGAGA | 3360 |
| $\mathcal{O}$   | TAAGGAAGC  | TAAAATGGAG | AAAAAATCA  | CTGGATATAC | CACCGTTGAT | 3420 |
|   | GGCATCGTAA | AGAACATTTT | GAGGCATTTC | AGTCAGTTGC | TCAATGTACC | 3480 |
|   | CCGTTCAGCT | GGATATTACG | GCCTTTTTAA | AGACCGTAAA | GAAAAATAAG | 3540 |
|   | ATCCGGCCTT | TATTCACATT | CTIGCCCGCC | TGATGAATGC | TCATCCGGAA | 3600 |
|   | CAATGAAAGA | CGGTGAGCTG | GTGATATGGG | ATAGIGȚICA | CCCTIGITAC | 3660 |
|   | TGAGCAAAC  | TGAAACGTTT | TCATCGCTCT | GGAGTGAATA | CCACGACGAT | 3720 |
|   | TTCTACACAT | ATATTCGCAA | GATGTGGCGT | GTTACGGTGA | AAACCTGGCC | 3780 |
|   | AGGGTTTAT  | TGAGAATATG | TTTTCGTCT  | CAGCCAATCC | CTGGGTGAGT | 3840 |
|   | TGATTTAAA  | CGTGGCCAAT | ATGGACAACT | TCTTCGCCCC | CGTTTTCACC | 3900 |
| <b>61</b> :   | TTATACGCA  | AGGCGACAAG | GTGCTGATGC | CGCTGGCGAT | TCAGGTTCAT | 3960 |
| (')   | TGATGGCTT  | CCATGTCGGC | AGAATGCTTA | ATGAATTACA | ACAGTACTGC | 4020 |
| < :   | 299992999  | GTAATTTTTT | TAAGGCAGTT | ATTGGTGCCC | TTAAACGCCT | 4080 |
| ( )   | TCTCTAGCT  | TGAGGCATCA | AATAAAACGA | AAGGCTCAGT | CGAAAGACTG | 4140 |
|   | TIATCIGIT  | GTTTGTCGGT | GAACGCTCTC | CTGAGTAGGA | CAAATCCGCC | 4200 |
| $\vdash$  | CCCTCCCCC  | GTTTCGGTGA | TGACGGTGAA | AACCICIGAC | ACATGCAGCT | 4260 |
| G   | TCACAGCTT  | GTCTGTAAGC | GGATGCCGGG | AGCAGACAAG | CCCGTCAGGG | 4320 |
| (')   | GTGTTGGCG  | GGTGTCGGGG | CGCAGCCATG | ACCCAGTCAC | GTAGCGATAG | 4380 |
| ø   | CTGGCTTAA  | CTATGCGGCA | TCAGAGCAGA | TTGTACTGAG | AGTGCACCAT | 4440 |
| <a href="#">1 · · · · · · · · · · · · · · · · · · ·</a> | AAATACCGCA | CAGATGCGTA | AGGAGAAAAT | ACCGCATCAG | GCGCICIICC | 4500 |
| H   | CACTGACTC  | GCTGCGCTCG | GTCTGTCGGC | TGCGGCGAGC | GGTATCAGCT | 4560 |
| $\mathcal{O}$   | GGTAATACG  | GTTATCCACA | GAATCAGGGG | ATAACGCAGG | AAAGAACATG | 4620 |
|   | GCCAGCAAAA | GGCCAGGAAC | CGTAAAAAGG | CCGCGTTGCT | GGCGTTTTTC | 4680 |

| GAGGTGGCGA 4740        |            | GCTCT 4800 | CT 480<br>TG 486  | T 480<br>G 486<br>G 492 | 480<br>486<br>492<br>98 | 4 4 8 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 | 4 8 8 0 4 4 8 8 0 4 4 8 8 0 0 1 2 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 | 4880<br>4986<br>4987<br>5048<br>510<br>510 | H 488 C C C C C C C C C C C C C C C C C C | T C C C T G G T T C C C C C C C C C C C | G C C C C C C C C C C C C C C C C C C C | 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 | 4 4 4 4 6 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 | 4 4 4 4 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 | 4 4 4 4 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 | 4 4 4 4 6 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 | 4 4 4 4 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 | 4 4 4 4 6 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 | 4 4 4 4 6 7 7 7 7 7 8 9 9 9 9 9 9 9 9 9 9 9 9 9 9 | 4 4 4 4 4 6 6 6 7 6 7 6 9 9 9 9 9 9 9 9 1 1 1 1 1 1 1 1 1 1 1 | 4 4 4 4 6 7 7 7 7 7 8 9 9 9 9 9 9 9 9 9 9 9 9 9 9 | 4 4 4 4 6 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 | 4 4 4 4 6 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 | 4 4 4 4 4 6 6 6 6 7 6 6 6 6 6 6 6 6 6 6 | 4 4 4 4 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 |
|------------------------|------------|------------|-------------------|-------------------------|-------------------------|---|---|--|---|---|---|---------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|
| AAGCTCCCT<br>TCTCCCTTC | TCTCCCTTC  |            | TOTARGETORI. TORC | GCGCCTTATC CGGT.        | TGGCAGCAGC CACT         | TCTTGAAGTG GTGG                         | TGCTGAAGCC AGTT.  | CCGCTGGTAG CGGT                            | CTCAAGAAGA TCCTTTGA                       | GTTAAGGGAT TTTG                         | AAAAATGAAG TTTT                         | AATGCTTAAT CAGT                       | CCTGACTCCC CGTC                         | CTGCAATGAT ACCG                         | CAGCCGGAAG GGCC                         | TTAATTGTTG CCGG                         | TIGCCATIGC TACA                         | CCGGITCCCA ACGA'                        | GCICCIICGG ICCI                                   | TTATGGCAGC ACTG   | CTGGTGAGTA CTCA                                   | GCCCGGCGTC AATA                         | TIGGAAAACG TICT                         | CGATGTAACC CACT                         | CTGGGTGAGC AAAAACAGGA                   |
| AAAAATCGAC             | TTTCCCCCTG | CIGICCGCCT | CTCAGTTCGG        | CCCGACCGCT              | TTATCGCCAC              | GCTACAGAGT                              | ATCTGCGCTC  | AAACAAACCA                                 | AAAAAAGGAT                                | GAAACTCAC                               | CTTTTAAATT                              | GACAGTTACC                            | TCCATAGCTG                              | GGCCCCAGTG                              | ATAAACCAGC                              | ATCCAGTCTA                              | CGCAACGTTG                              | TCATTCAGCT                              | AAAGCGGTTA  | TCACTCATGG  | TTTTCTGTGA  | AGTIGCICIT                              | GTGCTCATCA                              | AGATCCAGTT                              | ACCAGCGTTT                              |
| CGAGCATCAC             | ATACCAGGCG | TACCGGATAC | CTGTAGGTAT        | CCCCGTTCAG              | AAGACACGAC              | TGTAGGCGGT                              | AGTATTTGGT  | TIGATCCGGC                                 | TACGCGCAGA                                | TCAGTGGAAC                              | CACCTAGATC                              | AACTTGGTCT                            | ATTTCGTTCA                              | CITACCAICI                              | TTTATCAGCA                              | ATCCGCCTCC                              | TAATAGTTTG                              | TGGTATGGCT                              | GTTGTGCAAA  | CGCAGTGTTA  | CGTAAGATGC  | GCGGCGACCG                              | AACTTTAAAA                              | ACCGCTGTTG                              | TTTTACTTTC                              |
| GCCCCCCTGA             | GACTATAAAG | CCCIGCCGCT | AATGCTCACG        | TGCACGAACC              | CCAACCCGGT              | GAGCGAGGTA                              | CTAGAAGGAC  | TIGGTAGCTC                                 | AGCAGCAGAT                                | GGTCTGACGC                              | AAAGGATCTT                              | TATATGAGTA                            | CGATCTGTCT                              | TACGGGAGGG                              | CGGCTCCAGA                              | CTGCAACTTT                              | GTTCGCCAGT                              | GCTCGTCGTT                              | GATCCCCCAT  | GTAAGTTGGC  | TCATGCCATC  | AATAGTGTAT                              | CACATAGCAG                              | CAAGGATCTT                              | CTTCAGCATC                              |
| CATAGGCTCC             | AACCCGACAG | CCTGTTCCGA | GCGCTTTCTC        | CTGGGCTGTG              | CGTCTTGAGT              | AGGATTAGCA                              | TACGGCTACA  | GGAAAAAGAG                                 | TTTGTTTGCA                                | TTTTCTACGG                              | AGATTATCAA                              | ATCTAAAGTA                            | CCTATCTCAG                              | ATAACTACGA                              | CCACGCTCAC                              | AGAAGTGGTC                              | AGAGTAAGTA                              | GIGGIGICAC                              | CGAGTTACAT  | GTTGTCAGAA  | TCTCTTACTG  | TCATTCTGAG                              | AATACCGCGC                              | CGAAAACTCT                              | CCCAACTGAT                              |

| 6300  | 6360  | 6420  | 6480  | 6501         |
|---|---|---|---|--------------|
| ACTCATACTC  | CGGATACATA  | CCGAAAAGTG  | TAGGCGTATC  |              |
| AATGTTGAAT  | GTCTCATGAG  | GCACATTTCC  | CCTATAAAAA  |              |
| CCGCAAAAAA GGGAATAAGG GCGACACGGA AATGTTGAAT ACTCATACTC 6300 | AATATTATTG AAGCATTTAT CAGGGTTATT GTCTCATGAG CGGATACATA 6360 | TITAGAAAAA TAAACAAATA GGGGTTCCGC GCACATTTCC CCGAAAAGTG 6420 | TCTAAGAAAC CATTATTATC ATGACATTAA CCTATAAAAA TAGGCGTATC 6480 |              |
| GGGAATAAGG  | AAGCATTTAT  | TAAACAAATA  | CATTATTATC  | U            |
| CCGCAAAAAA  | AATATTATTG  | TTTAGAAAAA  | TCTAAGAAAC  | TICGICITCA C |
| AGGCAAAATG  | TICCITITIC  | TTTGAATGTA  | CCACCIGACG  | ACGAGGCCCT   |